REMARKS

1.1. The Examiner has advised us that the March 26, 2004 amendment to the specification could not be entered because the referenced passages do not correspond to the currently filed specification. This, in turn, resulted in the maintenance of two objections to the specification (present OA §§13 and 14).

We printed out the specification of record from the PTO Image File Wrapper, and found that most, although not all, of the March 26, 2004 amendments to the specification in fact corresponded to the currently filed specification. The instructions identified the amended paragraphs by the page and line number at which each began. Please note that in this specification, the line numbering is only of text lines, blank lines are ignored. Thus, the paragraph bridging pages 3-4 ("A broad aspect...") begins at page 3, line 31.

The following prior amendments were correct as previously stated, and hence have simply been repeated here (the reference is to the line on which the amended paragraph(s) begin(s)):

P6, L5
P6, L16
P8, L21
P14, L24
P22, L21
P22, L24
P22, L26
P22, L28
P28, L6
P28, L9
P28, L31.

The amendments at P3, L31, and P15, L24 were correct as previously stated, but we have further amended these paragraphs to supply antecedent basis for "isolated" in claim 5. We have newly amended the paragraph beginning at P17, L30 for the same

reason.

The amendment previously directed to P7, L24 should have been directed to P7, L23. This has been corrected.

We found that there were two inconsistent prior amendments directed to P30, L3 (page 9 of old amendment) and P30, L4 (page 12 of old amendment). This has been corrected.

Likewise, we found that there were two inconsistent prior amendments directed to P32, L30 (page 11 of old amendment) and P32, L32 (pages 12-13 of old amendment).

In view of the amendments, the objections set forth in OA §§13 and 14 should be withdrawn.

1.2. The 112/2 rejection of claims 31 and 32, by reason of their reference to Figs. 8A-8J, is respectfully traversed.

Applicants have amended claims 31 and 32 to recite the conserved tryptophans depicted in Figs. 8A-8J. The rejection is mooted by the amendment.

1.3. The term "contics" (P27, L30) is not a misspelled word. It is a term of art referring to a cluster of well defined genes.

1.4. The term "non-naturally occurring" has been removed from claim 5 and hence amendment of the specification to recite it is not appropriate.

2. Anticipation

2.1. Claims 5, 7 and 10 stand rejected (OA §16-18) as anticipated by Melgosa, et al. (1993), because Melgosa, et al. teach that they have isolated a 98 kDa protein band from the outer membrane complex of chlamydia pneumoniae, which they presume contains a single protein.

Applicants previously amended these claims to require that the claimed protein be "free of any other chlamydial protein" (not "product" as implied by the Examiner). Applicants previously argued that Melgosa et al.'s 98 kDa protein band is impure, based on literature evidence that several 98 kDa C. pneumoniae proteins exist. See pp. 21-22 of the March 26, 2004

response, supported by Vandahl et al. (2001) and the first Birkelund Declaration. Clearly, the formation of a single MW band under SDS-PAGE is inadequate evidence of homogeneity when several proteins from the source material are known to have similar MWs.

The Examiner nonetheless asserts that it is merely Birkelund's opinion that the Melgosa 98 kDa ligand contains a plurality of different chlamydial proteins. We would say that it was of course, an informed and expert inference based on hard evidence, i.e., the known molecular weights of the C. pneumoniae proteins studied by Vandahl et al.

The Examiner suggests the presentation of "extrinsic evidence" that Melgosa et al.'s 98 kDa band can be resolved into multiple components. Toward this end, we respectfully submit the second Declaration of Svend Birkelund, enclosed, and copies of the literature cited therein.

2.2. Claims 27-33 are newly rejected (OA §24) as anticipated by Melgosa, et al. This rejection is traversed for the reasons advanced with respect to base claim 5.

3. Written Description

The Examiner raises written description issues with regard to

(a) the limitation "non-naturally occurring protein"

(b) the coverage of the peptides of paragraph (ii) of claim 5, i.e, those comprising subsequences of Omp2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22 and 24 which in turn comprise a T cell epitope.

3.1. The specification plainly contemplates proteins which are not identical to the isolated (i.e., naturally occurring) Omp proteins.

Thus, at page 10, lines 5-23, the specification teaches

> When used in connection with proteins according to the present invention the term "variant" should be understood as a sequence

> of amino acids which shows a sequence similarity of less than 100% to one of the proteins of the invention. A variant sequence can be of the same size or it can be of a different size as the sequence it is compared to. A variant will typically show a sequence similarity of preferably at least 50%, preferably at least 60%, more preferably at least 70%, such as at least 80%, e.g. at least 90%, 95% or 98%.
>
> The term "sequence similarity" in connection with sequences of proteins of the invention means the percentage of identical and conservatively changed amino acid residues (with respect to both position and type) in the proteins of the invention and an aligned protein of equal of different length. The term "sequence identity" in connection with sequences of proteins of the invention means the percentage of identical amino acid with respect to both position and type in the proteins of the invention and an aligned protein of equal of different length.

The Examiner will appreciate that while some sequences which are, say, 50% similar to a disclosed OMP will happen to also occur in nature, the great majority of these sequences will be non-naturally occurring mutants.

Likewise, the specification discloses subsequences of the lead proteins, see page 10, lines 24-34, as well as polypeptides comprising such subsequences see P17, L30-P18, L2.

Again, while a few such polypeptides (other than the disclosed Omp proteins) will already exist in nature, the vast majority of these proteins will be non-naturally occurring.

Thus, Applicants were clearly in possession of "non-naturally occurring" variants and fragments of Omp4-15.

Nonetheless, we have decided that the limitation "isolated" (which the examiner did not question) is sufficient protection against inadvertently reading upon a product of nature, and have therefore excised "non-naturally occurring", mooting this rejection.

3.2. We turn next to the issue of descriptive basis for the

T-cell epitopes in clause (ii) of claim 5. As we understand the rejection, the Examiner acknowledges that applicants contemplated polypeptides consisting of subsequences of the recited Omp proteins, which subsequences in turn comprise T cell epitopes. If the Examiner disagrees, we respectfully refer him, e.g., to P17, L30-P18, L2:

> It is envisioned that particularly interesting and immunogenic epitopes will be found in connection with the proteins of the invention, which will comprise subsequences of said proteins. It is preferred to use polypeptides comprising such subsequences of the proteins of the invention in immunizing a mammal, such as a human, against chlamydia *pneumoniae*.

Rather, the Examiner contends that there is no disclosure of particular T cell epitopes, particular subsequences, or particular structures to be conserved. Hence, the Examiner says, we have failed to practically identify the claimed genus.

Vas-Cath requires that the description convey the invention, with reasonable clarity, to those skilled in the art.

Each of the 12 proteins which are completely disclosed by applicants reads on clause (ii) of claim 5, as each is an isolated chlanydial protein, and each necessarily comprises a T cell epitope.

By conveying the sequences of these 12 proteins, Applicants also conveyed with reasonable clarity, the T cell epitopes, as those skilled in the art would logically use sequence analysis software or systematic fragment testing to identify T cell epitopes. See pp. 23-26 of the March 26, 2004 amendment.

We appreciate that the written description and enablement requirements are "severable" (OA page 18). However, when the written description rejection alleges that the problem is with the artisan envisioning a detailed chemical structure, as opposed to failing to state that the chemical is of interest in the first place, then the written description analysis requires inquiry in what the artisan would infer, based on the appropriate skills,

from the disclosed structures (here, the full-length sequences).

4. New indefiniteness issues (OA §23)

4.1. The point regarding "non-naturally occurring" is moot as that term has been excised.

4.2. The subsequence in question is a subsequence, at least six amino acids in length, of any one of "said isolated proteins", which are recited in clause (i). Claim 5 has been amended to make this explicit.

4.3. The plural form ("proteins) is used when referring back to clause (i), which recites 11 different proteins.

4.4. The "said isolated proteins" at the end of claim 5 clearly refers back to clause (i) because it is part of the definition of the proteins of clause (ii). Nonetheless, this has been made explicit.

4.5. "The protein or peptide of claim 5", as recited in claims 27-33, may be either the protein of clause (i) or the one of clause (ii) (or both). We don't see how this is a problem.

Respectfully submitted,

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Enclosures
-Svend Birkelund Declaration
-Knudsen (1999)
-Vandahl (2001)
-Vandahl (2002)

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